

REMARKS

I. STATUS OF THE CLAIMS.

Claim 47 is presently pending. Claims 1-46 were previously canceled without prejudice to subsequent renewal. Claim 48 has been canceled without prejudice to subsequent renewal, including in a divisional or continuation, with entry of this amendment.

II. OBJECTION TO THE SPECIFICATION AND AMENDMENTS TO THE SPECIFICATION.

The specification was objected to because the status of the co-pending applications cited at page 18, lines 20-25 and the serial numbers for the co-pending applications cited at page 60, line 24 and page 61, lines 2 and 7 have not been provided. This objection has been overcome by amending the specification on page 18 to provide the additional identifying and status information and serial numbers for the applications cited in the specification as originally filed and requested by the Examiner. Applicants have also amended the specification on pages 60 and 61 to provide the serial numbers of the cited co-pending applications, as requested by the Examiner. No new matter is introduced by any of these amendments.

The specification was also objected to because it allegedly contains an embedded hyperlink and/or other form of browser-executable code at page 12, line 12. This objection is traversed in part and overcome in part. Applicants do not intend that this web address be an active link in any related published patent or published application. Thus, this link can be disabled by the Office when preparing the text to be loaded onto the USPTO web database. As indicated in MPEP § 608.01, where Applicants do not intend a hyperlink to be an active link (*i.e.*, such that the link becomes a live web link in the published patent or published application when placed on the USPTO web page), the Examiner should not object to the hyperlink and the hyperlink need not be deleted from the specification because the Office can disable the hyperlink when preparing the text to be loaded onto the USPTO web page. Nevertheless, in an effort to expedite prosecution, Applicants have amended the specification to remove this web address. Withdrawal of the rejection is respectfully requested.

The specification was also objected to as allegedly failing to provide proper antecedent basis for the claimed subject matter pursuant to citing 37 § CFR 1.75(d)(1) and MPEP §

608.01(o). Specifically, the Examiner states that “[c]orrection of the following is required: ‘recursive sequence recombination’.” Office Action, p. 3. Applicants respectfully traverse this objection. Under 37 § CFR § 1.75(d)(1), the claims must conform to the invention as set forth in the specification and the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description. Proper antecedent basis for the phrase “recursive sequence recombination” in Claims 47 and 48 is provided throughout the specification, including at, but not limited to, *e.g.*, page 17, lines 20-31. Support for this phrase was also indicated in Appendix C attached to the Amendment and Response to Restriction Requirement filed on March 27, 2003.

Applicants thank the Examiner for her close review of the specification. Pursuant to the Examiner’s request, Applicants have reviewed the specification and have corrected inadvertent typographical errors on pages 11 and 16. These amendments do not introduce any new matter and are merely undertaken to correct inadvertent typographical errors.

III. REJECTIONS UNDER 35 USC § 112.

Claims 47 and 48 were rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. The rejection of Claim 48 has been rendered moot by cancellation of this claim. The rejection of Claim 47 is traversed in part and overcome in part as follows.

Applicants respectfully traverse Part (A) of the rejection in its entirety. In support of the rejection, the Examiner takes the position that:

Claims 47 and 48 are confusing. The preamble recites “an optimized modulatory effect on immune response prior to optimization”. The body of the claim does not seem to recite an optimizing step. The method steps seem to lack essential step, i.e. step of an optimized modulation of polynucleotide. It is not clear in which of the only two steps of creating and screening, the step by which an optimized polynucleotide is obtained.

Office Action, pp. 3-4.

Applicants respectfully disagree. First, Claim 47 should not include a "step of an optimized modulation of polynucleotide" as suggested by the Examiner, because polynucleotides are not "modulated." Applicants respectfully submit the Examiner has misread the claim. Furthermore, Claim 47 does not lack any essential step. Claim 47, for example, is directed to a method for obtaining an optimized immunomodulatory polynucleotide (or polypeptide encoded therefrom) that has an optimized modulatory effect on an immune response as compared to a response prior to optimization. The method comprises creating a library of recombinant polynucleotides and screening the library to identify an optimized recombinant polynucleotide (or polypeptide encoded thereby) that has a modulatory effect on an immune response induced by a vector, wherein the optimized recombinant polynucleotide (or polypeptide encoded thereby) exhibits an enhanced ability to modulate an immune response compared to a polynucleotide from which the library was created. Specifically, the optimized recombinant polynucleotide encodes a co-stimulator selected from B7-1 (CD80) or B7-2 (CD86), and the screening step involves selecting variants with altered activity through CD28 or CTLA-4, and optimization is achieved by recursive sequence recombination.

The steps of the method of Claim 47 are clearly defined and would be readily understood by one of ordinary skill in the art. One of skill would certainly understand how to carry out the method defined by Claim 47 and would recognize that performing the recited method would result in obtaining an optimized immunomodulatory polynucleotide or polypeptide encoded thereby. No essential step is missing. Moreover, none of the terms of Claim 47 is confusing. On the contrary, the terms of the claim are clear and unambiguous and would be plainly understood by a skilled artisan.

With regard to Part (B) of the rejection, the Examiner finds that Claim 48 is a duplicate of Claim 47. This rejection has been overcome by the cancellation of Claim 48 without prejudice to subsequent renewal.

For at least these reasons, Applicants respectfully request withdrawal of the § 112 rejection.

IV. REJECTIONS UNDER 35 USC § 103.

Claims 47 and 48 were rejected under 35 USC § 103(a) as allegedly being unpatentable over Torigoe *et al.*, Abstract, *Peptide Chemistry: Proceedings of the 33rd Symposium on Peptide Chemistry* 405- 408 (1996) [hereinafter "Torigoe"] in view of US Patent No. 5,811,238 issued to Stemmer [hereinafter "Stemmer"]. The Examiner takes the position that the teachings of Stemmer in combination with those of Torigoe render Claims 47 and 48 obvious. The rejection of Claim 48 has been rendered moot by cancellation of that claim. The rejection of Claim 47 is respectfully traversed as follows.

Applicants respectfully submit the Action has not established a *prima facie* case of obviousness of Claim 47 based on the teachings of either Stemmer or Torigoe – taken alone or in combination. Three requirements must be met for a *prima facie* case of obviousness. First, the cited references must teach all of the limitations of the claims. MPEP § 2143.03. Second, there must be some particular suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine their teachings to produce the claimed invention. *Id.* Third, it must be demonstrated that there is a reasonable expectation of success of carrying out the claimed invention based on the teachings of the cited references. *Id.* The teaching or suggestion to combine and the reasonable expectation of success must both be found in the references themselves and not based on Applicants' disclosure. *Id.*

Applicants respectfully submit the Examiner has not explicitly shown how Torigoe or Stemmer or the combination thereof taught or suggested all of the limitations of Claim 47. Nor has the Examiner pointed to any particular suggestion in either Torigoe or Stemmer to combine its teachings with the other reference to produce the method as specifically defined by Claim 47. A suggestion to combine the reference teachings must be particularly shown in the cited references themselves by particular factual findings. *See, e.g., In re Anita Dembiczak and Benson Zinbarg*, 50 USPQ2d 1614, 175 F. 3d 994 (Fed. Cir. 1999). A suggestion to combine the teachings of various references cannot be assumed or simply postulated without explicit evidentiary support. In the present case, neither Torigoe nor Stemmer provides any motivation to combine its teachings with the teachings of the other reference. Finally, the Examiner has not sufficiently demonstrated there would be any reasonable expectation of success of carrying out the method of Claim 47 based on the

teachings of the two cited references. Thus, none of the three requirements for a *prima facie* case of obviousness has been met.

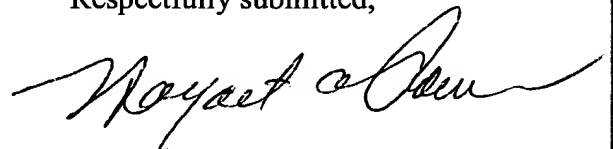
For at least these reasons, Applicants submit the rejection of Claim 47 under § 103 is improper and respectfully request that it be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. Applicants respectfully request that the Examiner contact the undersigned upon so finding, so that an interview may be scheduled with an interference specialist to discuss the Request for Interference which Applicants are presently preparing.

If there are any questions concerning this paper, or the application in general, the Examiner is invited to telephone the undersigned at (650) 298-5809 at her earliest convenience.

Respectfully submitted,



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